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Constructing 'exceptionality': a neglected aspect of NHS rationing

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Abstract:	<p>In the British NHS the principle of exceptionality involves assessing whether a patient is sufficiently different from the generality of patients to justify providing a treatment, such as an expensive cancer drug, not approved for routine funding. In England, individual requests for certain high-cost treatments are considered by local panels that examine exceptionality alongside treatment efficacy and cost as the main criteria for funding. This was also the case in Wales until September 2017. Our paper draws on audio recordings of panel meetings and interviews in a Welsh Health Board to investigate how exceptionality was constructed in discussions. It focuses on the problematic combination of different decision criteria in meeting talk, particularly regarding the discourses associated with efficacy and exceptionality. Exceptionality is a fluid category that raised questions about the evidence-based nature of panel decision making. In particular, the paper discusses the use of subgroup data from RCTs and the difficulty of deciding how small a subgroup of patients should be before it is deemed exceptional. Determining exceptionality has been an important mechanism for deciding that a minority of NHS patients can still receive high-cost treatments not routinely provided for all. As a neglected rationing mechanism it warrants sociological examination.</p>

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Abstract

In the British NHS the principle of exceptionality involves assessing whether a patient is sufficiently different from the generality of patients to justify providing a treatment, such as an expensive cancer drug, not approved for routine funding. In England, individual requests for certain high-cost treatments are considered by local panels that examine exceptionality alongside treatment efficacy and cost as the main criteria for funding. This was also the case in Wales until September 2017. Our paper draws on audio recordings of panel meetings and interviews in a Welsh Health Board to investigate how exceptionality was constructed in discussions. It focuses on the problematic combination of different decision criteria in meeting talk, particularly regarding the discourses associated with efficacy and exceptionality. Exceptionality is a fluid category that raised questions about the evidence-based nature of panel decision making. In particular, the paper discusses the use of subgroup data from RCTs and the difficulty of deciding how small a subgroup of patients should be before it is deemed exceptional. Determining exceptionality has been an important mechanism for deciding that a minority of NHS patients can still receive high-cost treatments not routinely provided for all. As a neglected rationing mechanism it warrants sociological examination.

(Abstract 200 words)

(Main text and references 9354 words)

This paper explores an important, but little-researched facet of healthcare rationing in the NHS in England and Wales concerned with the principle of 'exceptionality'. While there is a considerable body of research on macro aspects of health technology assessment (HTA), including the work of the National Institute for Health and Care Excellence (NICE) and its use of clinical effectiveness and cost-utility analysis in technology appraisals, less has been written about the institutional and procedural arrangements used to apply this framework at local level. This is important because in England certain treatments are only made available when patients successfully claim that they are 'exceptions' to policies that preclude routine provision of these treatments to the wider population. The position was the same in Wales until September 2017 when the principle of exceptionality was replaced by updated criteria of significant clinical benefit and reasonable cost (see discussion section). Thus the English panels that consider requests from patients and their doctors to fund these high-cost treatments, consider exceptionality alongside clinical efficacy and cost in determining whether to approve funding, as was the case in Wales until recently. Exceptionality refers to a situation where a patient is seen to be different from the generality of cases with a given condition to the extent that agreed policy on the non-provision of a treatment does not apply. It provides a mechanism for doctors to assert that patients would benefit from receiving an expensive treatment, such as a high-cost drug, even though it is not recommended for routine NHS funding by NICE.

This form of rationing remains highly controversial, with a recent BMJ investigation finding that numbers of funding requests received by English panels increased by 47% in the four years to 2017 (Iacobucci, 2017). While there is a small decline in funding requests in Wales, the health boards approved a similar number of requests for cancer

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3 medicines compared with previous years (AWTTC, 2018). England launched a
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5 consultation exercise on Individual Funding Requests (IFR) policy in October 2016 and
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7 published new guidance in November 2017 (NHS England 2017a; NHS England, 2017b),
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9 while NHS Wales published an independent review report and new guidance in 2017,
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11 on what are known there as individual patient funding requests (IPFR) (NHS Wales
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13 2017a; NHS Wales, 2017b). The exceptionality criterion came under fire in both
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15 countries, with critics questioning the validity of its application in the absence of a full
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17 technology appraisal or in the context of rare diseases (Heale and Syrett, 2018;
18
19 Routledge, 2017). The new English guidance left the existing decision-making process
20
21 largely unchanged, while NHS Wales now requires panels to look for greater than
22
23 average benefit only when technology appraisals are available, and has dropped the
24
25 term “exceptionality” from official guidance. Controversy continues on both sides of the
26
27 border so that case studies of the how panels construct exceptionality are highly
28
29 relevant to the ongoing policy debate.
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38 Exceptionality had emerged as an important concept in the early 2000s at a time when
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40 the nature of rationing was changing with the development of the NHS internal market
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42 under Prime Ministers Blair and Brown (Syrett, 2007). Older forms of implicit
43
44 rationing, through non-transparent professional judgement or waiting lists, were being
45
46 challenged and to some extent displaced by explicit rationing in the form of practices
47
48 such as exclusions lists and disinvestment in low-priority services (Locock, 2000; Syrett
49
50 2003). Mechanic (1997: 46) had predicted that explicit rationing might increasingly
51
52 become an administrative mechanism disconnected from clinicians. Syrett (2007: 55)
53
54 argues that as the internal market evolved after 1997 there was a shift of responsibility
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56 for allocative decision making away from individual doctors to groups of managers and
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professionals. He suggests that this was accompanied by an increasing focus 'upon the development of normative and/or technical criteria to underpin allocative decision making, and the establishment of procedures or institutions through which such decisions can be made' (2007: 54). The institutions and procedures concerned included NICE (established in 1999), clinical directorates and use of specialty guidelines and protocols in hospitals, and various types of 'priorities' committees in NHS purchasing organisations which operationalise national policies through backstage allocative decisions (Calnan, 2018). However, alongside this general push towards decisions based on explicit criteria, there was a realisation of the need to re-engage clinicians in order to ensure that this more transparent approach to resource allocation had a wide impact (Locock 2000: 97). According to Syrett (2007:55) exceptionality was a mechanism introduced to maintain legitimacy by allowing the possibility for individual clinical judgements to 'override managerial or political guidelines on allocation'.

Legal scholars trace the principle of exceptionality back to the judge's ruling in *R v North West Lancashire Health Authority, ex p A, D & G*, a 1999 judicial review case where the plaintiffs challenged a Primary Care Trust's refusal to fund gender reassignment surgery on the basis that there was no overriding clinical need or other 'exceptional circumstances'. The judge held that it was lawful for a health authority to adopt a policy of non-provision that allowed for exceptions in 'exceptional circumstances, even while leaving those circumstances undefined' (see: Ford, 2013: 28). Further legal underpinning for NHS commissioners to implement such policies was provided by Ministerial directions made under powers conferred by s.8 of the National Health Service Act 2006, and s.12 of the National Health Service (Wales) Act 2006. In the Welsh NHS discussed in this paper, the arrangements whereby patients and the

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3 physicians could make funding requests for consideration by Local Health Boards were
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5 set out in series of Welsh Government communications. By the time of the Richards
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7 Report, English Primary Care Trusts and Welsh Local Health Boards were using a
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9 variety of processes to deal with such requests (see: Richards 2008: 19, para 2.3), and
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11 one consequence of the report was convergence towards a common system of internal
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13 decision-making panels staffed by managers and professionals. These were variously
14
15 known as Individual Funding Request (IFR) Panels, Clinical Priorities Committees,
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17 Commissioning Advisory Groups, Effective Use of Resources Groups and, in Wales,
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19 Individual Patient Commissioning (IPC) Panels, but as time went by a process based on
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21 IFR/IPC panels emerged. The Welsh IPC panel that is discussed later in this paper was
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23 established in 2008 as this occurred.
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30 As the HTA system associated with NICE developed, commissioning bodies established
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32 panels and developed ethical frameworks and locally-agreed procedures to guide their
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34 decision making. In a companion paper (Hughes and Doheny, 2019) we examine how a
35
36 Welsh panel seeks to enact a form of evidence-based medicine, paying particular
37
38 attention to the pragmatic determination of clinical effectiveness (or “efficacy”) under
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40 conditions where definitive evidence is often absent. The present paper focuses on the
41
42 part of panel deliberations concerned with exceptionality, and thus touches on an area
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44 previously neglected by social science researchers. The few published studies that
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46 provide ethnographic accounts of IPC or IFR panels at work (Hughes and Doheny, 2011;
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48 Russell and Greenhalgh, 2012; 2014; Russell, Swinglehurst and Greenhalgh, 2014) tell
49
50 us little about how panels determine exceptionality in individual case discussions. To
51
52 date this topic has been left to scholars interested in law and bioethics (Ford, 2012;
53
54 2013; Syrett, 2007; Newdick, 2005; 2006; 2007).
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Yet apart from the issues of legitimacy touched on in the legal literature, rationing in funding panels has important sociological dimensions. The meaning of categories such as exceptionality – and the associated decision rules and boundaries – is negotiated in social interaction, and shaped by persuasive discourse and actors' attempts to align action with organisational work imperatives (Light and Hughes, 2001; Prior, 2001; Griffiths, 2001). The present study adds to a related strand of sociological research (Griffiths and Hughes, 1994; Hughes and Griffiths, 1996; Hughes and Griffiths, 1997; Russell and Greenhalgh, 2012; Russell and Greenhalgh, 2014) that suggests that rationing deliberations draw upon both expert and general cultural knowledge, and combine discursive repertoires and associated prioritisation criteria in complex ways. In particular, we examine how consideration of exceptionality alongside efficacy sets up tensions that required constant interactional work to manage. Despite a sustained attempt to bring the two principles within a common framework, these tensions raised doubts about the objectivity of the decision making process, and ultimately – in Wales at least – resulted in an attempt to decouple assessment of benefit from the principle of exceptionality.

Methods

Our IPC data come from a larger project on NHS contracting in England and Wales (Hughes, et al., 2011a; 2011b). The IPC fieldwork took place between April and October 2008. Eleven IPC panel meetings were attended by one of two researchers, involving 23 referred cases (some discussed in two or three meetings). Observation of IPC meetings was supplemented by attendance at three policy review panels (which considered appeals), interviews with key panel members and examination of relevant background

documents. NHS research ethics committee approval and access approval from the health board were obtained, and all panel members signed consent forms (see: Hughes, 2018, for a discussion of ethical issues raised by the study).

Apart from preparing a single early paper (Hughes and Doheny, 2011), we did not fully analyse the IPC data at the time of the study. This was partly because we needed to give priority to findings on mainstream secondary care contracting in the two countries to satisfy our funder, but also because of legal complications that made our audio-recorded data sensitive. A patient whose funding request was denied sought judicial review, and we were asked to provide the associated audio recordings for possible use in court (Hughes, 2018). The fact that our data are now some ten years old is an acknowledged weakness of the present analysis, but – as mentioned above – the individual funding request process remains highly topical, particularly in regard to exceptionality. Given the paucity of observational studies of a hard-to-research aspect of NHS work we believe that the present analysis still has value.

The IPC meetings were transcribed in full and the transcripts analysed paying attention to both the sequential organisation of talk and emergent themes. This may be seen as a form of linguistically-sensitive ethnography, building on earlier studies that have sought to ground interactional studies more firmly in detailed sequences of spoken interaction (Cicourel, 1968, Strong, 1979; Silverman, 1987).

The setting for the study was a single LHB located on a trading estate in a medium sized Welsh city. All but one of the panel members were health board employees. The panel was chaired by the health board Medical Director, and attended by the Assistant Director of Commissioning (ADC), Finance Director (FD), Director of Clinical

Development (DCD), Assistant Director Clinical Development (ADCD), IPC officer (IPCO), and a pharmacist advisor (PA). The latter was a hospital pharmacist who was subcontracted part-time to support the IPC panel. Meetings were held on every second Tuesday morning (with some breaks in the summer due to absences for holidays) around a large table in the office of the Director of Clinical Development. Names used in the analysis are pseudonyms.

The data extracts presented here were selected from our 31 recorded case discussions (involving 23 patients) because they provide clear exemplifications of certain themes emerging from the fieldwork. In only a small number of case discussions where efficacy was said to be absent was exceptionality not discussed, but we acknowledge that only a small number of cases fall within certain of the categories considered in our analysis. The picture emerging may thus be a partial one, which for example did not include any case discussions relating to rare diseases, but the paper describes ways of constructing exceptionality that we would expect to be repeated in many meetings.

Agreeing a decision-making process

The Local Health Board's ethical framework for individual patient commissioning stated that high-cost treatments not presently commissioned would only be funded when the IPC panel determined that the intervention was both effective and there was reason to believe the patient was more likely to benefit than the population of patients of that type (that the patient was exceptional). The shift of focus that occurred as the panel moves from discussing efficacy to determining exceptionality may be seen as the point where an evidence-based discussion of what works changed to take account of available

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resources. Since most funding requests related to drugs that had not received NICE approval, efficacy was usually considered in relation to published evidence from randomised controlled trials (RCTs) showing how far the drug was effective for particular groups of patients. Discussions did not usually touch on cost-utility analysis that might suggest that a drug with some degree of efficacy nevertheless could not be provided because it exceeded NICE’s cost-effectiveness threshold (the Incremental Cost Effectiveness Ratio [ICER] of between £20,000 and £30,000 per quality-adjusted life year [QALY] gained that typically applied). The shift from considering what worked to considering what could realistically be provided, was delayed until the issue of exceptionality was raised. The logic of panel deliberations was that a drug not approved for routine NHS use would indeed not be efficacious for most patients, and that only those who have atypical characteristics associated with greater than average benefit could be considered for funding within a constrained health board budget. Thus the test of exceptionality was the mechanism used to limit access to high-cost treatments, and the point when a rationing process became visible.

Our observations began when a new IPC panel had been operating for less than two months. The decision process was still evolving and we observed two meetings when panel members discussed the proper order for consideration of efficacy and exceptionality. The decision procedure that emerged was that as a first step the panel would assess whether the intervention was efficacious, and only then, and as a second step, would the panel consider whether the patient was exceptional.

Extract 1

MD: But I want to know whether we as a panel agree that that's the way that we look at things. Whether we look at efficacy first and if it's not effective we don't look at exceptionality. That is what I would like everyone's agreement on really.

DCD: We need to just check though all of our decisions have been made on that because I am not quite sure.

MD: Well I know that all mine have.

PA: A lot of them have been. What I am saying is...all I am saying is there is a lot of grey ones. There's ones where we all went mmmm...

DCD: Well there is always going to be grey wherever process and...

PA: What you are saying is hundred per cent my opinion... I agree with what you are saying.

MD: Is it right?

PA: Yes.

MD: I think even though the consultants come back

DCD: Can I just bring up the Cetuximab patient.

PA: The one we agreed.

DCD: From Crossways. How did she get through on exceptionality if it wasn't efficacious?

MD: Well it wouldn't.

DCD: It would have had to have done. How did we get into... If we are saying... If it is not efficacious, we never look at exceptionality, how did we make the decision for that woman that she was exceptional? We have turned down other Cetuximab that must have been... it's not efficacious. So how have we gone into the exceptionality? I just...

MD: What? Was she found exceptional?

DCD: If that is a principle?

PA: Age and the aggressiveness of her cancer because it all happened within a very short space of time.

DCD: If we are saying that, it is not efficacious and therefore exceptionality does not apply. She should not have had that. I'm sorry.

MD: Was that my patient? I wasn't in on the decision was I?

DCD: I am just...that was...yeah...that's the one I can remember we have not applied that principle.

MD: I wasn't...

DCD: We have gone down the exceptionality route...we have gone down... the drug wars

MD: Because I have always applied that you see. I have always...that's the order I have always done it in.

(IPCP, May 20th)

The decision about sequencing was highly consequential because it determined how two distinct prioritisation criteria could be combined and incorporated into a decision-making process that would be used to structure the format of meetings. In this extract panel members reason that a drug that cannot be shown to be efficacious should not be funded. The Medical Director, who had excused herself from an earlier meeting because she felt it necessary to declare an interest, says that then considering exceptionality led

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3 to a wrong decision. Yet as the above discussion shows, there were cases where the
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5 panel found it difficult to separate the case discussion into two stages according to this
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7 sequence. We will return to this issue later.
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10 11 **Science or pragmatism?** 12 13

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16 When talk turned to exceptionality this was usually the point in meetings where a
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18 discourse that emphasized science and research evidence took a pragmatic turn to
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20 acknowledge resource constraints. NHS funds are insufficient to provide general
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22 funding for drugs that are not cost-effective enough to meet NICE's ICER threshold, but
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24 Health Boards have capacity to fund a limited volume of exceptional cases and so
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26 determining exceptionality becomes the selection mechanism. Surprisingly there was
27
28 rarely prolonged discussion of cost as such, and panel members stated on several
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30 occasions that no funding requests had been denied on cost grounds. Nor was there
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32 overt mention of social worth or personal biography. Rather, on the surface at least,
33
34 exceptionality was linked to scientific evidence. Typically, exceptionality was inferred
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36 from published evidence from RCTs that showed greater than average benefit for a
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38 defined subgroup of patients in which the referred patient appeared to fall. The panel
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40 continued to interrogate the same research papers that they had used to establish
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42 efficacy for evidence about relative benefit for different patient subgroups. Where there
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44 was clear extra benefit for a small subgroup of atypical patients that might
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46 simultaneously establish efficacy and exceptionality. The difficulty was that using
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48 research evidence relating to efficacy to establish exceptionality sometimes involved a
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50 kind of logical leap that raised doubts about scientific validity in the minds of panel
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members. The pharmacist advisor, the panel member most involved in the assembly of evidence, was particularly sceptical.

I don't know what exceptionality means. I really don't. (...) It's catch 22 from the point of view of the evidence. On one hand they are saying you shouldn't use sub-group analysis because the evidence isn't strong. So if you have got a study that says "oh yeah this drug is fantastic we are not commissioning it because we don't know if it is cost-effective. And then, well, we will look at exceptionality". We start going into sub-groups then and I find that quite hard because some place...also I'm aware that some local health boards don't look at the evidence they look at the exceptionality and that's all they look at. (...) I really believe with exceptionality if you had different panel meetings on different days of the week, I think you would come up with different decisions about what you consider exceptional. [...] The exceptionality bit, I'm not convinced of that personally. (Interview, pharmacist advisor)

One perceived problem where panel members already felt that research evidence pointed towards general efficacy, was that they then still had to find grounds for saying that a patient was different from most other patients. A second problem concerned just how small a subgroup needed to be before patients within it could be deemed exceptional. We will consider these in turn.

When proof of efficacy is not proof of exceptionality

The first of the above problems came up when the panel determined that recent research shows that a drug benefitted a wide range of patients, and then needed to find evidence not just that the referred patient was likely to benefit, but benefit more than the general population. Panel members found themselves searching for a way to describe patients that constructed them as different from the generality of cases and to show that this was associated with greater benefit.

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6 In the following extract the panel begins by exploring whether a patient diagnosed with
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8 non-small cell lung cancer and liver metastases has the same characteristics as patients
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10 shown in a randomised controlled trial to derive benefit from the drug Tarceva
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12 (Erlotinib). The BR21 trial found that overall survival for patients taking Tarceva was
13
14 6.7 months, compared with 4.7 months for those receiving a placebo (Shepherd et al,
15
16 2005). The pharmacist says that at face value the patient meets the inclusion criteria
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18 for the trial. By the time this extract begins the panel have already had a lengthy
19
20 discussion of the likely benefit of two extra months of life. The decision problem here
21
22 involves first agreeing that this is sufficient benefit to constitute meaningful efficacy,
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24 and then considering whether the patient has characteristics that might mean she
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26 derives greater than average benefit. The trial provided no specific data for patients
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28 with renal metastases, something that might have provided grounds for exceptionality.
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30 The discussion then moves to the information from the referral letter that the lung
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32 tumour has been surgically removed via a lobectomy, which is what the consultant says
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34 makes the case an exception. Although the panel does not appear to have agreed on the
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36 degree of efficacy found, it moves on to talk about whether the lobectomy makes the
37
38 patient an exception. Although the panel does not appear to have agreed on the
39
40 degree of efficacy found, it moves on to talk about whether the lobectomy makes the
41
42 patient an exception.
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45 Extract 2

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47 PA: It would have been stage three before, which as far as I am aware is metastatic, with
48
49 performance status nought to three. So she meets that criteria and she has had one or
50
51 more chemotherapies. She meets all inclusion criteria for the study.

52 MD: Right.

53 PA: Then we are back into the overall survival is six point seven months versus four
54
55 point seven months with best supported care. Five per cent of patients discontinued
56
57 because of toxicity and most of them are rash as far as I can see.

58 MD: So it's an extension of two months.

59 PA: The bit that makes it different is that she has had it [i.e. the lung tumour] whipped
60
out. None of these people would have had...I presume...I could be wrong now...

MD: Is there any evidence that compares outcomes? I am sure there is loads. But any evidence that compares outcomes with and without lobotomy. Lobectomy.

PA: I am going to say no because I have read this loads and loads of times and I was under the impression that people that had advanced disease didn't have...

MD: So they don't do a lobectomy with advanced....

PA: I presume they are so far into the disease that they don't get to that stage. Its sounds like she was lucky to get a lobectomy

MD: So what we don't know is whether having had that lobectomy earlier... if will affect her outcome now

PA: No idea. That's possibly where she doesn't fit this criterion.

MD: That's what she is stating is the exceptionality.

PA: Yeah.

MD: Because with exceptionality. The criteria for exceptionality has to mean that they lie outside the general population and in so doing benefit more than the average patient.

PA: Well, you could argue that maybe the lobectomy makes her lie outside the norm.

The liver mets is five per cent but I found a figure of three point eight per cent....

MD: But it's not just lying outside it's lying outside in such a way that they would benefit more.

PA: What I can't tell you is whether this lady is going to benefit more than the usual. That I can't tell you.

MD: So in that way she doesn't constitute exceptionality then. Because although she lies outside she is not necessarily going to benefit more.

(IPCP, April 29th)

In this extract the Medical Director points to the likely two months extension of life shown by the trial as evidence of efficacy. Although in past discussions some panel members had expressed doubt about whether this gain was enough to lead NICE to approve the drug, the fact that they move on to discuss exceptionality here suggests that they accept that the drug is efficacious, if only for a limited time. The consultant has claimed that the case is exceptional because of the lobectomy, the removal of the primary tumour that is unusual in stage three lung cancer cases. While assembling evidence of efficacy often depends on a pragmatic judgement of probable benefit (see: **Hughes and Doheny, 2019**), greater than average benefit is even more difficult to demonstrate, and the pharmacist hedges his answers with uncertainty markers ("I presume", "you could argue"). Panel members decide that in the absence of evidence that this type of surgery improves outcomes for those receiving Tarceva, they cannot say that the patient is exceptional. The panel agree that the pharmacist will double

check that no such evidence exists. In the event none was found and funding was denied.

In an interview completed a few days later the Medical Director shed further light on her thinking about this case.

MD: Sometimes I'm conscious that what we are trying to do is to... when I'm not sure whether to count something as effective or not in terms of their length of extra life, you know if it is only two months, I suppose it makes it an easier decision if I kind of know whether there is any exceptionality. And it is probably. And I am aware actually that I think I did that before maybe more than I do now because I think there are definite stages that you have to go through and if you try and do the two together it complicates it. I think from what you were saying I was trying to work out whether this lady was exceptional...whether there were any elements of exceptionality there, and if it was effective... if we decided that two months was effective it would make a difference. It is easier to say that something is not effective if you know that you are not going to fund it anyway. I think that's the honest truth, you need to be much more clear thinking than that. I think you do have to sit and put exceptionality to one side and say do we consider this is effective or not. Do we consider two months extra life for this lady constitutes...is this effective? I think it is hard. [...] I needed to kind of think well should we be funding this you know... by saying two months isn't effective are we actually depriving this person of treatment? Let's actually have a look and see if there is anything exceptional.

Int: Sneaking a look at exceptionality?

MD: I was sneaking a look.
(Interview, Medical Director)

Here we see the tensions that emerge when an empiricist repertoire, based on clinical effectiveness evidence, rubs against a "procedural" repertoire, concerned with limiting funding to a subset of patients (for a discussion of these repertoires see: Hughes and Doheny, 2019). Use of two separate tests of eligibility could lead panel members to vacillate between consideration of sameness and difference, and in doing so raise doubts about whether they were really engaged in evidence-based decision making. In this interview the Medical Director acknowledges that the life and death nature of the decisions weighs heavily and may encourage the panel to sneak 'a look' at exceptionality

when evidence of efficacy is unclear. She concedes that although 'there are definite stages that you have to go through', there are instances in hard cases where the panel fails to follow that sequence.

Subgroups and percentages

The second issue that came up in many cases concerned how large a subgroup had to be before patients in it ceased to be exceptional. The following example involves a patient with renal cell carcinoma whose consultant requested Sunitinib (a tyrosine kinase inhibitor) on the basis that she was unable to take the standard cytokine-based therapy, Interferon Alfa and is exceptional because she is in the intermediate prognostic group. The notion of the intermediate prognostic group comes from a risk stratification model used to assess prognosis, mainly for inclusion in clinical trials, based on the Memorial Sloan-Kettering Cancer Center scoring system. Patients in the intermediate group have 1 to 2 of 5 identified risk factors and a predicted median survival of 10 months. This category came up frequently in renal cell carcinoma cases, as more patients fall within it than in the good and poor risk groups.

In the extract below, panel members consider evidence from a recent trial examining the relative efficacy of the two drugs published in the New England Journal of Medicine (Motzer et al., 2007). For the intermediate prognostic group, this study found that median survival for 209 patients taking Sunitinib and 212 patients taking Interferon was 11 months and 4 months respectively, a clearer benefit than was shown for the good and poor risk groups (the intermediate group comprised 421 of 750 patients studied).

Extract 3

ADC: He hasn't given this lady Interferon?

PA: No. He says she is intermediate prognostic group.

MD: She can't take it. But that's why we need to know the percentage of patients who can't take it.

PA: Well, all I can tell you is the numbers that were put into the trial. Providing they are representative...

MD: Yes, but there must be figures on how many patients come into an intermediate prognostic group, mustn't there? So that we can say... give some idea...

DCD: I am not quite sure you would have statistics around how many with renal cell would come into an intermediate category.

MD: Well, they must know how many you can't use Interferon on. If it is as clear as that so "these patients don't benefit from Interferon", we must have some figures around that? [Pause 11 seconds] This is a particularly difficult morning, isn't it?

DCD: The day's not going to get any easier.

PA: Fifty-five per cent.

MD: Sorry James, what did you say?

PA: The Frenchay* have looked at this and come up with a figure of fifty-five per cent within an intermediate prognostic group for cytokine efficacy which... Fifty five per cent... which holds out very similar to the figures included in the study.

MD: Right.

PA: Fifty per cent I would have said of the patients in the study were in the ... 421 patients out of 706 were in the intermediate prognostic group.

MD: Right.

PA: 750, sorry.

MD: So this patient is not an exception.

DCD: No.

MD: Because she is in that group of fifty-five per cent. Is that right? Do you want to check on it or is that?

PA: Yeah, I'm happy to check on it.

MD: Or are you happy...are you confident with that?

PA: This is a paper that says not to use.

FD: [inaudible phrase] are you worried about the timescale here?

PA: I have got to read this

MD: You have got to read right? So can we say – do you want time to – if it's fifty five per cent. [...] Do you want more time James or do you think that that's actually as good as you'll get?

PA: I think it's going to be as good as we'll get.

*The Frenchay Hospital, Bristol

(IPCP, May 20th)

Again panel members struggle to translate the RCT evidence into the percentages needed to determine above-average benefit. The published paper contains no information on the proportion of the intermediate risk group unable to benefit from

Interferon, and the best the pharmacist can provide is the fifty-five per cent estimate from a Bristol research group. The panel reason that if around half of those in the same diagnostic group as the referred patient might benefit, then the patient is not exceptional, and funding was denied.

The intermediate treatment group itself was said to account for about half of renal cell carcinoma cases and the panel was consistent in the meetings observed in deciding that patients falling in this (large) subgroup were not exceptional. As can be seen from the next extract, it appeared that good, intermediate or poor prognostic group was always too large a category to be relevant, even though several consultants entered these categories on the referral form as grounds for exceptionality.

Extract 4

ADC: We discounted prognostic factors in that first decision didn't we?

MD: Yeah.

PA: Because no no no we dropped it out because it was good and good is forty per cent. Therefore it wasn't exceptional. Now this is intermediate.

DCD: Right.

MD: That's fifty per cent.

PA: And actually intermediate is fifty per cent so that is not exceptional either. (IPCP, June 24th)

Nevertheless, reference to subgroups other than prognostic group often came up when exceptionality was being considered, and it was unclear exactly where the line would be drawn. We explored this issue in an interview with the Medical Director.

If it was forty-nine per cent would you call that exceptional? I don't know what legally would be called exceptionality. You know, would benefit more than the average... You know, what does that mean in legal terms? I mean from what I have seen of judicial reviews it is usually pretty small. It can't be unique. It can't be because I think one of the judicial reviews wasn't passed because...wasn't won or the patient won because the LHB had used such strict criteria for exceptionality that it had to be unique and that they felt that was not fair. So it obviously has to be a number but how big that number is is tricky.

(Interview, Medical Director)

This response illustrates how judicial review was a constant preoccupation for panel members, and had resulted in a widespread view that seeing exceptionality in terms of unique characteristics would be an overly stringent test that was probably unlawful. However, the working assumption that a subgroup needed to be 'pretty small' to establish exceptionality, left the panel with a zone of indeterminacy where outcomes depended more on judgement than science.

Searching for exceptionality

Panel members frequently complained that clinicians did not understand exceptionality. Syrett (2007) suggested that exceptionality provided a channel for continued clinician influence over treatments for individual patients, but this was not evident in our study. For example, the panel would frequently find fault with the way consultants completed the section of the request form detailing the reason for exceptionality. Sometimes this resulted in denial of funding, but in several cases panel members replaced what they took to be the consultant's weak claims about exceptionality with a more convincing construction of their own. Often this meant building a complex chain of reasoning that sought to marshal scientific evidence in a way similar to how efficacy was established. The following extract concerns another renal cell carcinoma case, again involving an ineffective first-line cytokine-based therapy, interleukin-2.

Extract 5

MD: Just to check then. So he failed – this is a failed Interleukin-2. So what percentage do we know of patients...

PA: No idea. Sorry.

MD: So that's where we go with the exceptionality I would imagine unless there are any other factors? Do you think it is likely to be...exceptional?

PA: The way it is written down here as exceptional, "the patient has failed to respond to high dose Interleukin-2. If a patient has failed Interleukin-2 will not respond to Interferon".

MD: We need to know percentages.

[passage omitted]

DCD: We need some evidence as to why we should consider this case on the basis of exceptionality. There isn't. We haven't got anything in front of us.

[passage omitted]]

MD: No. No. I mean I think we're right to do exceptionality. Is there anything else that we could consider as exceptional other than Interleukin-2?

PA: First diagnosis was June she has been quite aggressive... well I say aggressive – short time scale.

MD: Good prognosis, good prognostic factors.

PA: Good performance score.

MD: So we need to know the percentages of that don't we? If she is more likely to benefit than the average if that's a smaller percentage.

ADC: How accurate are they James? Because if they are subjective...

PA: I think it is in the pile of papers I've got out there, there's a whole tranche of things that ehm...

ADC: It's how do you measure them...

PA: It's very much along the lines of if you are lying in bed and you are not moving then you've got poor prognostic factors. It's also the size of the tumour and all sorts of things like that.

MD: Wouldn't it be...

PA: Have you had it removed? She has had hers removed. She's got mets but she's got a good performance score. The prognostic factors do - although they are very simple - do correlate well in renal cell carcinoma with outcome, as in helping to live longer.

MD: So it's histology as well as patient's general health?

PA: Yeah, the performance score is one of them.

MD: Right, right. Okay. So we could. It would help wouldn't it? I mean it would be a measure.

ADC: I'm just wondering are they comparative from patient to patient? Cos if we are looking for exceptionality then we are looking for absolute percentages. Are they comparable? Because if they are not comparable that's...

MD: If they are using the same factors they will be comparable.

ADC: I just wondered if there was an element of subjectivity in it.

PA: Yes, there is.

(IPCP, June 24th)

Here panel members consider a series of factors that might indicate exceptionality, but encounter the problem that most are not measureable in a way that would allow comparison with the generality of patients for whom the drug is not funded. As explained in our companion paper (Hughes and Doheny, 2019), panel deliberations

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2
3 differ from the discourse of the typical medical consultation in that a case is generally
4 considered in relation to trials data on the relevant condition-based risk group, rather
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6 than its unique clinical characteristics. The preoccupation with percentages and
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8 measurement reflects the increasing societal importance of statistical reasoning, often
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10 in the context of cost control or regulation (Porter, 1995), and not least in the context of
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12 evidence-based medicine (Tonelli, 1998; Greenhalgh et al., 2015). Even in that part of
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14 deliberations concerned with efficacy, sample or population-based statistics are
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16 frequently interpreted in terms of averages without attention to range or distribution,
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18 but even this fuzzy match between individual patient and trials data may be absent
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20 when exceptionality is considered. In the above exchange panel members point to a
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22 complex picture that includes metastases, a good performance score, and partially
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24 unknown risk factors, but cannot find evidence that early surgery will make the drug
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26 more beneficial. They agree there is an 'element of subjectivity' that the science does
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28 not remove.
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38 **Blurring efficacy and exceptionality**

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40 Authorities in the field of evidence-based medicine warn against drawing conclusions
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42 from outcomes calculated for subgroups in RCTs, on the basis that post-hoc analysis of
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44 differences that a trial was not powered to detect is likely to be unreliable (Brookes et
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46 al., 2001; Rothwell, 2005). Panel members were aware that subgroup analysis should
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48 be used cautiously, and mainly in cases where observation of differential outcomes had
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50 emerged from multiple trials or was derived from appropriately-designed studies. Yet
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52 members found themselves continually pushed into discussion of subgroups, even
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54 when supposedly still assessing efficacy. Arguably this was an inevitable result of the
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56 decision problem that they faced. Several drugs under consideration had been
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appraised but not approved by NICE or All Wales Medicine Strategy Group (AWMSG), on the basis that they were not efficacious or cost effective for the general patient population. Yet funding might still be considered in individual cases. This meant that the panel generally started from the assumption that research would not show sufficient general benefit, but might nevertheless show benefit for some patients with atypical characteristics.

The consequence, when efficacy was established by using subgroup analysis, was that it became difficult to maintain a sharp conceptual distinction between efficacy and exceptionality. This was an issue with the renal cell carcinoma patient discussed in Extract 3 above. The consultant argued that the patient was exceptional because she fell into the intermediate prognostic group, and the NEJM trial showed greater benefit for this group than for the good and poor risk groups. However, during the panel discussion of efficacy the pharmacist observes that in talking about risk group members are moving into the questionable domain of subgroup analysis (the 'realms of ropiness'). The MD points out that if they are considering efficacy on the basis of subgroup data, the panel is already in effect considering exceptionality.

Extract 6

PA: So you are talking eleven months versus four months. This is where we get into the realms of aah ropiness. So this is a sub-group analysis of the study

MD: Of the intermediate prognostic group

PA: Yeah. So you are talking seven months difference... in the study that we said earlier on. So the All Wales Medicine Strategy Group have turned it down, irrelevant of whether it is intermediate or good or poor prognostic factors. So the case that he is putting forward is that she fits into this intermediate group and therefore she would gain more benefit from it, because you can't use Interferon. Because you gain no benefit from that at all. And that seems to be held up by one of the references he's stuck in here.

MD: But how much? What percentage of patients come into that group?

PA: Don't know that

[...]

MD: But also we're getting into the realms of exceptionality aren't we? Without deciding first whether this is efficacious.

PA: We've got to get into the realms of sub-groups for this particular patient. It leads you into exceptionality because of the...because he has put in the intermediate prognostic factor.

MD: Because it is efficacious...in that group?

PA: In that one particular group. So he has led us down the path of exceptionality already.

(IPCP, May 20th)

As we saw earlier, this funding request was denied, but it was one of several cases that led panel members to reflect on whether they were blurring efficacy and exceptionality. In a subsequent interview the Assistant Director of Commissioning suggested that this was the kind of case that convinced her of the need to decide efficacy as the primary issue.

I used to blur the two and I think it makes it more difficult because that's one of the things that you learn when you go back and look at these cases again... is that if you have blurred the two it is harder to defend. You are much better being very clear. Let's just take exceptionality out, just let's consider efficacy. Let's decide on that first and although it is tempting to kind of...well let's just peep and see whether we would fund or not, it's not...it blurs it because you have blurred your decision about efficacy.

(Interview Assistant Director Commissioning)

In practice, however, this separation was not easily achieved. The blurring of the categories meant that even when it came to accounting for outcomes in written replies to funding requests there was the possibility of citing the absence of either efficacy or exceptionality as the reason for the decision. This meant that the choice of which to mention might depend on which was seen to offer the more defensible account. The following extract comes at a time when the panel had had to review a number of decisions after appeals from referring consultants, who had written back with additional evidence following a panel decision letter stating that a drug would not bring clinical benefit.

Extract 7

MD: Okay, so if it is not...if there is no evidence for it being effective then we don't need to look at exceptionality and we don't fund.

PA: I personally struggle with this bit because the counter argument that will come back - this is one view - that we view this as an effective treatment.

MD: Who do?

PA: Consultants, staff. Otherwise they wouldn't have requested it. I just think we are opening ourselves up to a letter stating that "I disagree with the..." and we will go "I disagree" and we will end up toing and froing

MD: But that is a problem we have got. Unless we agree with everything they say, we're always going to have that aren't we?

PA: Or we go down the exceptionality route and we say we can find nothing exceptional about it.

(IPCP, May 20th)

The idea that exceptionality might be used strategically as a means of heading off complaints from dissatisfied consultants illustrates the fluid nature of this category.

Although this was the only time we saw this happen in the observed meetings, the example suggests that exceptionality is not merely a principle for differentiating patients, but a way of justifying denial of funding in decision letters that is hard for consultants and patients to counter.

Discussion

In a companion paper (Hughes and Doheny, 2019) we argue that the form of evidence-based-medicine enacted in panels is shaped by wider organisational and political imperatives. Even with regard to that part of a panel discussion concerned with 'efficacy', the purity of 'the science' is eroded by the limitations of a pragmatic assembly of evidence in the limited time available, the evolving nature of NICE guidance, the difficulty of disentangling efficacy from cost-effectiveness, and the sometimes dubious use of subgroup data from RCTs. Where a line must be drawn between those who will receive a treatment and those who will not, it is inevitable that judgment as well as objective science is involved. This is reflected in a passage in the current All-Wales IPRF

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3 policy guidance that acknowledges that reasonable decisions are 'a compromise based
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5 on a balance between different value judgements and scientific (evidence-based) input'
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8 (NHS Wales, 2017: 10).
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12 At the time of our observations panel deliberations incorporated a combination of
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14 decision criteria, concerned with exceptionality, efficacy and cost, which frequently
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16 came into tension. Assembling these discursive elements in such a way as to keep
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18 discussions on track and create the appearance of a rational and fair decision-making
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20 process required sustained interactional work on the part of panel members, and it
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22 appeared that exceptionality was seen as the most difficult component to reconcile with
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24 evidence-based decision making. Exceptionality is a fluid category that can be
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26 constructed along multiple dimensions. Prior's (2001) study of cancer genetics clinics
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28 described how the designation of patients as high, intermediate or low risk, and
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30 consequent access to services, depended on a contingent 'assemblage' of assessment
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32 criteria that adjusted to the circumstances of the case. Just as high-risk or low-risk
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34 might be seen as categories 'on wheels', the meaning of exceptionality is highly
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36 malleable. As the pharmacist advisor complained in our interview, the principle might
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38 be interpreted differently by different Health Boards or constructed differently by the
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40 same panel at different times. We saw, for example, that doubts arose when considering
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42 whether subgroup evidence suggesting efficacy also established exceptionality, and
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44 regarding what percentage of a patient population had to fall within a subgroup for it to
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46 be deemed exceptional.
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57 The NHS landscape in Wales has changed considerably since our fieldwork was
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59 completed. The former IPC panels are now known as IPFR (individual patient funding
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request) panels, but remain similar to the English IFR panels. In the intervening decade the IPFR process provoked continuing controversy, involving *inter alia* dissent over denial of treatments, geographical variations in Health Board policies, Ministerial interventions, and the handling of rare diseases. New NHS Wales guidance issued in June 2017 no longer refers to exceptionality, but retains certain principles that resemble the previous framework. Funding of requested treatments that have not been subject to HTA now depends on new criteria of significant clinical benefit and reasonable cost. The reasonable value for money criterion will apply in all cases. However, where a NICE or AWMSG appraisal exists, approval will depend on the additional test of whether:

‘the patient’s clinical circumstances are significantly different to the general population of patients for whom the recommendation is not to use the intervention, such that {...} [t]he clinician can demonstrate that the patient is likely to gain significantly more clinical benefit from the intervention than would normally be expected from patients for whom the recommendation is not to use the intervention’ (NHS Wales, 2017: 12).

It is not clear whether panels will interpret ‘appraisal’ in this context to mean a final technology appraisal, so that significant judgmental discretion may remain in cases where interim guidance exists or the patient’s condition does not precisely match that covered by the guidance. In any event, this latter criterion suggests that many case discussions will not differ greatly from the ones discussed in this paper. Patients with rare diseases or requesting ‘non-NICE, non-AWMSG’ treatments may indeed benefit from escaping the test of exceptionality, but difference from the generality of patients

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will continue to be an issue in many cases where requests for high-cost drugs go to IPFR panels. This, in our view, is an inevitable consequence of the wider HTA framework associated with NICE, which accepts that public health care must necessarily be provided within the envelope of a global budget. A tax-funded NHS system operating within a spending limit is unable to provide all treatments that might bring some benefit, but by law must avoid blanket exclusions, and can only accomplish this by using some variant of the idea of difference from the norm. This suggests to us that science will inform but not remove discretionary decision-making in panels that will continue to operate within a web of organisational, cultural and political influences.

It is unclear whether the new Welsh approach will have any influence across the border, where funding still depends on exceptionality. The position in England changed somewhat following the establishment of the Cancer Drugs Fund in 2010, and its significant expansion in 2016, so that decision-making regarding the provision of certain drugs considered in this paper now often bypasses the IFR process. However, Ford (2013) predicted that this would lead to a greater number of non-cancer treatments going through the IFR process, (Iacobucci, 2017). Wales' New Treatments Scheme, launched in 2017, provides more limited access to high-cost medicines than the English scheme, but also seems to have resulted in some reduction in drug requests at the same time that non-drug requests are increasing (AWTTC, 2018). In this domain, as in several other areas of health policy, the contrasting approaches taken in England and Wales provide a valuable natural experiment that deserves future study.

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